REMARKS

Applicant submits this Amendment in response to the Office Action dated January 16, 2009. Reconsideration of the subject application as amended herein is respectfully requested. The Examiner is thanked for the various suggestions for response that were set forth by the Examiner in the Office Action.

Claims 1-15 are pending in this case, of which claims 8-10 are considered withdrawn as a result of applicant's earlier election of the Group I invention in response to a restriction requirement, thus leaving claims 1-7 and 11-15 for examination on the merits; of these, only claim 1 is independent. In the Office Action, all of the claims were rejected on statutory grounds, either as failing to meet the written description requirement or for indefiniteness, or on the basis of prior art. Specifically, the Examiner rejected claims 1-4, 6 and 12-15 under 35 U.S.C. §103(a) as unpatentable over du Breuil et al. in view of Sambrook et al. (both of which are non-patent references cited by the Examiner), and in addition, the Examiner rejected claims 5-7 and 11 under 35 U.S.C. §112, first paragraph, as being based on a non-enabling disclosure; moreover, all of the examined claims were rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The Examiner also raised a number of formal and substantive

objections to the text of the specification and claims, and to the drawings; an issue regarding the inventorship declaration was also raised.

In this amendment, applicant has canceled claims 1-10 (including withdrawn claims 8-10), as well as claims 12 and 14-15. Applicant is presenting new independent claim 16 (a generic claim which combines the features recited in former claims 1 and 2, and which also contains clarifying language as compared with former claim 1), and applicant is also presenting new dependent claims 17-19. The subject matter of new claims 17-18 corresponds to that of former claims 3-4, respectively, while the subject matter of new claim 19 combines the subject matter of former claims 5-10 into a single new, sub-generic, claim. The dependencies of remaining dependent claims 11 and 13, and the grammar in claim 11, have been adjusted accordingly. Applicant will endeavor to explain hereinbelow the basis on which applicant sincerely believes that claims 11 and 13, as presently amended, and new claims 16-19, are patentable over the cited prior art and are otherwise allowable.

Turning first to the issue raised by the Examiner concerning the inventorship Declaration, applicant submits herewith a new formal inventorship Declaration, which was executed by the sole inventor, Marcos Isamat Riviere, on April 14, 2009. The new

Declaration is compliant with 37 C.F.R. §1.67(a), and it identifies the present application by its application number and filing date.

Referring next to the Examiner's claim objections set forth on pages 2-3 of the Office Action, applicant has worded new claims 16-19, and applicant has amended remaining claims 11 and 13, so as to correct the informalities to which the Examiner objected. Specifically, the claims are now not only written in standard English, but are also now in compliance with U.S. patent practice. In addition, and as suggested by the Examiner, the preamble language has been corrected such that the independent claim recites "A method for ..." and the dependent claims recite, or have been amended to recite, "The method of claim ... ." Furthermore, although the Examiner's objection to the use of the term "cytoplasmatic" (a misspelling of "cytoplasmic") seems to have been limited to its appearance in some of the *claims*, applicant is also amending the specification, in a number of locations, in order to correct the same misspelling therein, and also to correct one other misspelling ("secuence") that was discovered. No new matter is being introduced.

Turning now to the claim rejections based upon 35 U.S.C. §112, first paragraph (as set forth on pages 3-4 of the Office Action), and to the related objections to the

specification and to the Sequence Listing, applicant seeks to correct the informalities noted, and to make the disclosure enabling, by amending the present application (as suggested by the Examiner) so as to add the entire nucleotide sequence of the human cytoplasmic beta-actin gene to both in the specification and the Sequence Listing.

In particular, applicant is amending the specification so as to add that nucleotide sequence in the form of a new drawing figure, namely, Figure 8, using a new sequence identifier "SEQ ID NO:9" to designate that reference sequence in accordance with 37 C.F.R. §1.821(c) and 37 C.F.R. §§1.822 and 1.823. Applicant is also adding a new paragraph on page 9 of the specification, containing a description of that new drawing figure in words, to be included in the brief description of the several views of the drawings for consistency. Inasmuch as that nucleotide sequence was impliedly incorporated into the specification by reference to the accession number under which it was submitted to the GenBank database, no new matter is being introduced by virtue of this amendment (as the Examiner recognized in the Office Action). The Examiner will note that the new sequence identifier "SEQ ID NO:9" has been used in new claims 16 and 19 to refer to either the entire nucleotide sequence of the human cytoplasmic beta-actin gene, or to particular nucleotide positions therein.

Since new Figure 8 is presented on a separate drawing sheet, applicant is submitting herewith a replacement set of *all* of the drawings for this application, consisting of eight (8) sheets, to replace the seven (7) sheets of existing drawings now on file. No changes have been made in existing Figures 1-7, although the numbering appearing at the top of each of the drawing sheets has been changed from "1/7," "2/7," etc. to "1/8," "2/8," etc.

In addition, as called for by the Examiner in the Office Action, and as required by the Rules of Practice, applicant is adding the same full nucleotide sequence of the human cytoplasmic beta-actin gene to the Sequence Listing for this case. Specifically, applicant is submitting herewith, and is amending this patent application so as to specifically direct the entry of, a revised Sequence Listing (in paper form), listing not only the eight nucleotide sequences in this application that were listed previously, but also a ninth nucleotide sequence comprising the entire DNA sequence of the beta-actin gene. The revised Sequence Listing, consisting of five (5) pages, replaces in its entirety the Sequence Listing previously submitted for this application, which consisted of only three (3) pages. Applicant is also submitting herewith a copy of the revised Sequence Listing in computer readable form (on a single CD-ROM), in accordance with the requirements of 37 C.F.R. §§1.821(e) and 1.824.

In connection with the revised Sequence Listing submitted concurrently herewith, applicant's undersigned counsel hereby states (1) that the content of the enclosed paper copy and the enclosed computer readable copy, submitted in accordance with 37 C.F.R. §§1.821(c) and (e), respectively, is the same, and (2) that the content of the information submitted herewith, in accordance with 37 C.F.R. §1.821(g), does not include new matter.

Regarding the Examiner's comments concerning the GenBank accession number, applicant advises that the specific version of the reference sequence that is being added to the present application is associated with accession number M10277.1, GI:177967. The date of deposit associated with this particular GI number is October 30, 1994, which clearly antedates the earliest priority date upon which applicant relies herein. As requested by the Examiner, applicant submits herewith a printout (screen capture) of the GenBank entry carrying that particular GI number.

Turning next to the claim rejections that were based upon 35 U.S.C. §112, second paragraph (as set forth on pages 4-7 of the Office Action), applicant believes that all of the claims, as presently amended and/or presented herewith, are no longer indefinite. Specifically, the claims now recite the step of "amplification" of segments of

the DNA of the beta-actin gene, without reference to PCR or to "an equivalent technique"; thus, the particular amplification technique to be utilized is not specified in the claims. Also, new independent claim 16 now includes a fourth step, and as such, is not missing the essential step in which the biological species is identified. Moreover, the claim now clearly conveys that either the sizes (in base pairs), or the actual DNA sequences, of comparable segments of the beta-actin gene from different organisms are compared; the comparison is made between the DNA taken from a sample derived from an unknown species, and a computer database containing information about the characteristics of the corresponding segments of the beta-actin gene of a plurality of known species.

The Examiner's comments concerning former dependent claim 3 have been taken into account in the wording chosen for new dependent claim 17, which recites that the amplification step is carried out using DNA *oligonucleotide primers* having evolutionary DNA sequence conservation *greater than 98%* between species and subspecies, thus rendering the claim definite. Support for the latter limitation may be found in the specification at page 6, lines 26-27. Similarly, the Examiner's comments concerning former dependent claim 4 have been taken into account in the wording chosen for new dependent claim 18, which clarifies that the segments to be amplified

comprise the whole intronic DNA sequence and at least a portion of the flanking exonic sequences, for each of the B, C, D and E introns, as those regions are annotated in the GenBank Record, thus rendering this claim definite as well.

The Examiner's comments regarding former dependent claims 5, 6 and 7 (on pages 5-6 of the Office Action) either have been remedied or have been rendered moot by the wording chosen for new dependent claim 19. Furthermore, the Examiner's comments (on pages 6-7 of the Office Action) regarding former dependent claims 12 and 14 and former independent claim 15 have been rendered moot by the cancellation of those claims.

Turning finally now to the rejections of the claims that were based upon prior art, claims 1-4, 6 and 12-15 were rejected under 35 U.S.C. §103(a) as unpatentable over du Breuil et al. in view of Sambrook et al. Applicant respectfully traverses this rejection, and contends that independent claim 16, as presented herewith, is distinguishable over, and is non-obvious in view of, the cited prior art, and that dependent claims 11, 13 and 17-19 therefore define patentable subject matter as well.

Du Breuil et al. report a simplified competitive PCR system based on

interspecies sequence differences and similarities, in order to study quantitative variations in hepatocellular carcinoma cells in response to serum addition. These authors exploit the existing, known nucleotide differences within exon 3 of the cytoplasmic beta-actin gene between humans and rats. The DNA in this exon is conserved between these two species except for some positions (in the third base of some codons, although this is not in shown in Figure 1 of the cited du Breuil et al. article), which vary between humans and rats, and create restriction sites in one species but not in the other, leading to a method that discriminates specifically between *those two species only*.

The Examiner's extrapolation that this, in itself, qualifies as a general method for identifying species is not sustainable, since although the DNA at some positions varies between humans and rats, some of this DNA is *conserved* between humans and other primates, as well as between rats and other rodent species; hence, it is useless as a universal approach to identifying biological species. Furthermore, the DNA fragment which is amplified, as described by du Breuil et al. is located within an evolutionary conserved exon, and for this reason there is no divergence in molecular weight (length in base-pairs) between species, rendering species discrimination impossible in heterogeneous samples consisting of tissue from more than one biological species, as

they would not be resolved universally by a restriction enzyme.

Furthermore, the Examiner's assertion that the basis for a universal species discriminatory approach is set forth when the teachings of du Breuil et al. are hypothetically combined with those of Sambrook et al. (particularly those in chapter 6, pp. 30-33, and chapter 14, pp. 10-11, as cited by the Examiner), and that these references when taken together would make such an approach obvious to one of ordinary skill in the art at the time of the invention, is not only a dubious interpretation at best, with no scientific basis in the evolutionary facts revealed by straightforward sequence comparisons, but is also an oversimplification of both the efforts of applicant and the innovative aspects inherent in the present invention.

Applicant's discovery that the capacity of the cytoplasmic beta-actin locus for universal species discrimination, as compared with other actin-family genes or other housekeeping genes, is not an obvious one, and has required laborious and time-consuming experimental determinations. Furthermore, another prior art reference already of record, which was brought to the Examiner's attention by applicant (but which was not relied upon by the Examiner in rejecting any of the claims) actually teaches *away* from considering the cytoplasmic beta-actin locus as a suitable region for species

discrimination.

Applicant refers specifically to the article by Bellis, C. et al. entitled "A molecular genetic approach for forensic animal species identification," which was published in 2003 in the journal Forensic Science International (vol. 134, no.2-3, pp. 99-108), and which was listed as a non-patent literature document in the Information Disclosure Statement that was submitted by applicant on June 23, 2008. A careful review of this article indicates that the authors considered the beta-actin gene as *not useful* as a tool for animal species identification. The article describes the species-discriminatory capacity of 5 unrelated genomic loci, including a region of the beta-actin gene. The authors state (on page 107) that "...this result was found to be too close to allow this method (beta-actin PCR) as an identification technique for forensic science investigations," and therefore they suggest that the use of the beta-actin locus be relegated to a minor role as follows: "... beta-actin could serve well as a positive control in PCR reactions to indicate that successful amplification has occurred."

Interestingly, both references, that of du Brueil et al., which dates from 1993, and that of Bellis et.al., which appeared ten years later, describe using exactly the same primers, presumably as a result of mere coincidence, since Bellis et al. do not cite du

Breuil et al. in their list of references. Whether coincidence or not, the region amplified in both references, consisting of a 289-bp segment of the beta-actin exon 3, is evolutionary conserved by virtue of belonging to an exon: the amino acid homology between humans and xenopus is 100%, and at the nucleotide level, there is 95% homology between humans and rats, and 90% homology between humans and xenopus. Thus, no divergence in molecular weight or in nucleotide (nt) sequence is to be expected in this highly conserved exon, and therefore its selection by du Breuil et al. as a candidate for species discrimination, even as between humans and rats *only*, was certainly not based on any evolutionary rationale. Accordingly, since a reading of Bellis et al. clearly teaches *away* from the use of the beta-actin locus for universal species discrimination, one of ordinary skill in the art would have recognized that du Breuil et al.'s teachings (even when combined with those of Sambrook et al.) were limited to the use of the beta-actin locus for discrimination between humans and rats, and the hypothetical person of ordinary skill would *not* have taken this teaching as a suggestion by du Breuil et al that the beta-actin locus should or could be used for more universal species discrimination.

On the other hand, the regions within the beta-actin locus disclosed by applicant (expressed using relative position numbers) are clearly distinct from those proposed by

du Brueil et al. and/or Bellis et al., and span intronic regions where there is very significant sequence divergence among various species. On this basis, applicant has recognized that the beta-actin locus *can* function as an attractive species-discriminatory molecular marker, despite the contrary teachings of the prior art.

In summary, the relevant prior art references indicate (erroneously) that the beta-actin locus is not suitable for universal species discrimination, and that the methods described therein rely on *exon sequence* species-specific variability for species discrimination. This fact is particularly relevant, since applicant's disclosure teaches exactly the opposite, namely, to rely only on 100% sequence homology between species in order to make the reaction applicable to ALL species (universal), and that the beta-actin lcous is suited for this purpose, as it is present and conserved throughout all forms of life. This evolutionary characteristic is rare for the majority of other loci, whose very existence in different types of organisms, let alone their nucleotide conservation, varies greatly, and this is not an obvious scientific realization. This finding has required lengthy and laborious evaluation of currently publicly available gene sequences, and has been proven thorough experimental taxonomic determinations of biological samples, which have already been performed in a collection of 344 species from over 1,200 individual biological samples, representative of all major animal taxa.

For all of the foregoing reasons, applicant contends that the choice of the beta-actin locus for universal molecular identification of biological species, as proposed in the present application, is not an obvious one, and that, as presently claimed, it is both novel and inventive. The rejection under 35 U.S.C. §103(a) should therefore be withdrawn.

In view of applicant's cancellation of claims 1-10, 12 and 14-15 (and despite the addition of new claims 16-19), the effective total number of claims in this application still does not exceed the number of claims covered by the basic filing fees initially paid, and the total number of independent claims still does not exceed three. Accordingly, applicant believes that no additional filing fees are required by virtue of the claim amendments made herein. Nevertheless, the Commissioner is authorized to charge any fee deficiency, or to credit any overpayment, to Deposit Account No. 07-1730.

In addition, the Commissioner is requested to construe this paper as including a retroactive petition for a three-month extension of time in which to file a response to the outstanding Office Action, and accordingly, the official fee of $1,110.00, as prescribed therefor by 37 C.F.R. §1.17(a)(3), as amended, in the case of a non-small entity, is submitted herewith. The Commissioner is again authorized to charge any additional

extension fees which may be required, or to credit any overpayment, to Deposit Account No. 07-1730.

Applicant has responded herein to the points raised by the Examiner in the Office Action, and applicant has amended the claims in an earnest effort to place this application in condition for allowance. Accordingly, further favorable action in connection with this patent application is earnestly solicited. The Examiner is invited to contact the undersigned attorney by telephone if it will advance the prosecution of this case.

Respectfully submitted,

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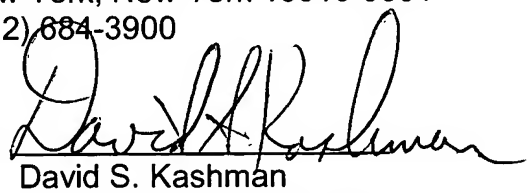
By: 
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CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on:

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July 9, 2009
(Date of Signature)